



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 300

[Docket No. FDA-2019-N-5553]

RIN 0910-AI36

Annual Summary Reporting Requirements Under the Right to Try Act

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA, the Agency, or we) is issuing a final rule to specify the deadline and content for submission of an annual summary of investigational drugs supplied under the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017 (Right to Try Act) and the uses for which the investigational drugs were supplied. This final rule implements a provision in the Right to Try Act that requires sponsors and manufacturers who provide an “eligible investigational drug” under the provisions of the Right to Try Act to submit to FDA an annual summary of such use, and directs FDA to specify by regulation the deadline of submission.

DATES: This rule is effective [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]. For additional information on the effective and compliance dates, see section V of this document.

ADDRESSES: For access to the docket to read background documents or comments received, go to <https://www.regulations.gov> and insert the docket number found in brackets in the heading of this final rule into the “Search” box and follow the prompts, and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240-402-7500.

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I. Executive Summary

A. Purpose of the Final Rule

The purpose of this rule is to implement provisions of the Federal Food, Drug, and Cosmetic Act (FD&C Act), added by the Right to Try Act, which requires sponsors and manufacturers who provide an “eligible investigational drug” under the Right to Try Act to submit to FDA an annual summary of such use, and directs FDA to specify by regulation the deadline of submission. The rule provides information on the necessary contents of the annual summary and the deadline for its submission.

B. Summary of the Major Provisions of the Final Rule

The rule adds a new subpart to the regulations, to specify the deadline and content for submission of an annual summary of investigational drugs supplied under the Right to Try provisions of the FD&C Act and the uses for which they were supplied. The Right to Try Act provides that the manufacturer or sponsor of an eligible investigational drug shall submit to FDA an annual summary of any use of such drug supplied under the FD&C Act. Per the statute, the

summary shall include the number of doses supplied, the number of patients treated, the use for which the drug was made available, and any known serious adverse events from use of the drug.

C. Legal Authority

The enacted provisions of the Right to Try Act, in conjunction with FDA's general rulemaking authority serve as FDA's legal authority for this rule.

D. Costs and Benefits

This final rule establishes the deadline for submission of annual summaries of use of investigational drugs supplied under the FD&C Act. The rule also establishes the required contents of these submissions.

The benefits of this rule consist of societal and public health outcomes that may accrue from the disclosure of the use of investigational drugs and any known serious adverse events provided in these annual summary reports. There is no data that would allow us to predict the magnitude of generated benefits, and thus we are unable to quantify the expected benefits of this rule.

Costs are estimated as the time spent by firms to prepare and submit these annual summary reports. The total estimated present value of this rule's costs is \$37,132 at a 7 percent discount rate and \$45,818 at a 3 percent discount rate. The annualized cost of this rule over 10 years is \$5,287 at a 7 percent discount rate and \$5,371 at a 3 percent discount rate.

II. Background

A. Need for the Regulation/History of the Rulemaking

On May 30, 2018, the Right to Try Act (Pub. L. No. 115-176) was signed into law, creating section 561B of the FD&C Act (21 U.S.C. 360bbb-0a). The Right to Try Act amends the FD&C Act to establish an alternative option for patients who meet certain criteria to request access to certain unapproved drug products and for sponsors and manufacturers who agree to provide those certain unapproved drug products, other than through FDA's expanded access

program.¹ This law provides a new pathway for patients to request and manufacturers or sponsors to choose to provide access to certain unapproved, investigational drugs, including biological products, for patients diagnosed with life-threatening diseases or conditions as defined in § 312.81 (21 CFR 312.81) who, as certified by a physician, have exhausted approved treatment options and who are unable to participate in a clinical trial involving the investigational drug.² This rule does not require that physician determinations be submitted to FDA. Manufacturers or sponsors who provide their investigational drug under the Right to Try Act are required to submit to FDA an annual summary of the use of their drug(s). Specifically, manufacturers or sponsors of an eligible investigational drug must submit to FDA an annual summary that includes the number of doses supplied of an eligible investigational drug, the number of patients treated, the uses for which the drug was made available, and any known serious adverse events. Per section 561B of the FD&C Act, FDA is required to specify, through regulation, the deadline for such submissions (section 561B(d)(1)). This rule specifies that deadline. This rule specifies that submissions must be made electronically. Currently, this means attaching a PDF document to an email. In the future, FDA may move to electronic submission through other direct means.

B. Summary of Comments to the Proposed Rule

FDA received fewer than 50 comments to the proposed rule from healthcare professionals, patient advocacy groups, regulated industry, scientific and academic experts, and private citizens. FDA received comments on the following: (1) the annual summary submission deadline; (2) the definition of “manufacturer”; (3) reporting information in the annual report on dosing, any known serious adverse events, clinical outcomes, patient demographic information, and the amount, if any, charged for the product; and (4) general comments requesting

¹ Information on FDA’s Expanded Access Program is available at <https://www.fda.gov/news-events/public-health-focus/expanded-access>.

² Physicians who have questions should consult with sponsors and manufacturers of eligible investigational drugs. Resources for determining whether there are available clinical trials include the sponsors of eligible investigational drugs and the website <https://www.clinicaltrials.gov>.

clarifications. FDA also received general comments both in support of and against the proposed annual reporting rule as well as the entire Right to Try Act.

C. General Overview of the Final Rule

FDA has extended the submission date for the first annual summary report from 60 calendar days after the final rule becomes effective as proposed to a specific date of March 31, 2023.

III. Legal Authority

The Right to Try Act amended Chapter V of the FD&C Act by inserting section 561B. New section 561B(d)(1) of the FD&C Act requires FDA to specify by regulation the deadline of submission of an annual summary of the use of any eligible investigational drug under the Right to Try Act by manufacturers or sponsors and specifies the contents of such summaries. This section, in conjunction with our general rulemaking authority in section 701(a) of the FD&C Act (21 U.S.C. 371(a)), serves as our legal authority for this final rule.

IV. Comments on the Proposed Rule and FDA Response

A. Introduction

We describe and respond to the comments in sections IV.B through IV.J of this document. We have numbered each comment to help distinguish between different comments. We have grouped similar comments together under the same number, and, in some cases, we have separated different issues discussed in the same comment and designated them as distinct comments for purposes of our responses. The number assigned to each comment or comment topic is purely for organizational purposes and does not signify the comment's value or importance or the order in which comments were received.

B. Description of General Comments and FDA Response

(Comment 1) Some comments made general remarks supporting or opposing the proposed reporting rule or Right to Try in general without focusing on a particular proposed

provision. These comments either supported or opposed the proposed rule, without any suggestions for specific changes.

(Response 1) FDA made no changes in response to these comments, as there were no suggestions for specific changes. In regards to comments opposing issuance of the proposed rule, we do not agree that FDA should not issue this rule. Section 561B(d) of the FD&C Act provides that “the Secretary shall specify by regulation” the deadline of submission of annual summaries. This rule implements the statutory directive in section 561B(d) of the FD&C Act, and FDA concludes that the rulemaking is necessary to establish deadline requirements for the submission of annual summaries.

C. Comments on the Submission Deadline

(Comment 2) Several comments focused on proposed § 300.200(b)(1) regarding the submission deadline. These comments requested a change of the submission deadline for the first annual summary from 60 calendar days after the rule becomes effective to 90 calendar days. Some comments also requested that the first annual summary cover a 12-month time period beginning from the finalization of the Proposed Rule onward. Some comments requested that for the initial annual summary, the reporting period should begin on the date the final rule is published and end on December 31 of that calendar year.

(Response 2) FDA agrees with the proposal to change the submission deadline for the first annual summary from 60 calendar days after the rule becomes effective to 90 calendar days. Regarding the proposals to change the reporting periods for the first required annual summaries, FDA disagrees that use of investigational drugs under the Right to Try Act prior to the finalization of this rule should not be reported. Rather than directing manufacturers or sponsors to only report Right to Try Act uses after FDA’s rulemaking is completed, the Right to Try Act directs manufacturers or sponsors to submit to FDA an annual summary of “any use” of a drug under the law (section 561B(d)(1) of the FD&C Act). Therefore, requiring submissions of Right to Try Act uses since enactment of the law is consistent with the statute. Furthermore, the

information in the reports may provide relevant information regarding the use of eligible investigational drugs. The comment's suggestion could lead to a situation where a serious adverse event that occurs 1 day prior to the final rule publication is not shared with FDA but the same event that occurred 2 days later is. Therefore, we are finalizing the proposed requirement that uses of eligible investigational drugs under Right to Try be reported to FDA, even if they occurred before issuance of this rule. The rule is considered in effect 60 days after the date of publication, however the due date for the first annual report is March 31, 2023 (see section V), but the Right to Try Act was effective as of the date it was signed, May 30, 2018. The rulemaking establishes the process for reporting actions sponsors already have taken. The first annual summary should cover all uses under the Right to Try Act since the statute has been in effect in accordance with § 300.200(b).

D. Comments on Combining Right to Try Reporting

(Comment 3) Several comments addressed combining Right to Try reporting with other FDA regulatory reporting requirements, noting that it may be less burdensome and facilitate FDA having all of the data on an investigational product together. Some comments requested the inclusion of the annual report on Right to Try uses as an addendum or section within the investigational new drug (IND) annual report required under § 312.33 (21 CFR 312.33), in addition to a separate report. Some comments requested aligning the Right to Try Act reporting with the annual reporting required under the Expanded Access regulations and aligning the reporting of known serious adverse events under proposed § 300.200(c)(5) with current serious adverse event reporting regulations under § 312.32 (21 CFR 312.32).

(Response 3) FDA disagrees with the comments requesting combining Right to Try reporting with other FDA-required reports. The IND reporting regulations do not capture all the information required under Right to Try, so it is not accurate that compliance with § 312.32 will provide compliance with the reporting requirements in this rule. Consequently, the information detailed for the Right to Try submission would have to be added to the IND annual report.

Moreover, existing IND annual reports under § 312.33 are due to FDA based upon the date an IND application was submitted to FDA. These IND annual reports are submitted throughout the year and not at a single point in time for all active applications, which is consistent with international harmonization efforts. It would be extremely difficult and resource-intensive for FDA to examine all IND annual reports for the sole purpose of identifying those potentially few reports that have Right to Try information so that we can compile the annual summary required by section 561B(d)(2) of the FD&C Act. In addition, it is efficient to have separate reporting requirements for Right to Try Act and other investigational drug uses because section 561B(c) of the FD&C Act limits FDA's use of clinical outcomes associated with the use of eligible investigational drugs under the Right to Try Act in ways that are not applicable to other uses of INDs. For these reasons, it is more efficient to implement the annual reporting and summary requirements of the Right to Try Act by requiring the annual reports to be submitted as separate reports to FDA.

FDA does not intend to object if sponsors refer to their Right to Try activities in their IND annual report required under § 312.33 as long as such information is labeled as Right to Try and is also included in the separate Right to Try annual report. The reporting requirements in § 312.33 include a provision that requires sponsors to identify the IND numbers that correspond to the products used under Right to Try. This will facilitate the integration into FDA systems and allow FDA to link all information received on a particular IND or new drug application or biologics license application.

E. Comments on Submitting Dosing Information

(Comment 4) Some comments made recommendations on proposed § 300.200(c)(2) regarding dosing. Section 300.200(c)(2) proposed to require that the annual summary include the total number of doses supplied by the manufacturer or sponsor to eligible patients for use under the Right to Try Act. We also proposed that each dose of an eligible investigational drug supplied for an eligible patient shall be counted as a dose supplied. Several comments

recommended that FDA require sponsors or drug manufacturers to report the number of doses per patient, rather than the cumulative number of doses supplied of the drug overall.

(Response 4) As noted in the proposed rule, FDA only proposed to require reporting on the total number of doses supplied. This will make the reporting requirements less burdensome for sponsors and is consistent with the requirements in the Right to Try Act, which does not require that information be submitted on a per patient basis. It is also consistent with our public health oversight needs, because at this time FDA does not foresee a need for more detailed information and FDA can follow up with the submitter if more information would be useful to FDA as it reviews the annual summary. However, sponsors may voluntarily provide an itemized list of doses per patient in their tabular summary when reporting any known serious adverse events; FDA encourages sponsors to include information on the number of doses supplied per patient when reporting on known serious adverse events even though this rule does not require this information.

(Comment 5) One comment expressed that the example given in the proposed rule of a tabular summary goes beyond the level of information required by the Right to Try Act.

(Response 5) FDA disagrees with the comment, because the tabular summary example included in the proposed rule showed information that sponsors may choose to submit to provide context around the known serious adverse event information. Specifically, the sample tabular summary that FDA provided in the proposed rule included such non-mandatory information as a field for a Patient ID number and for grading the severity of known serious adverse events. However, we did not propose to require that manufacturers or sponsors submit this information (and indeed the final rule does not require submission of such information).

To the extent the comment seeks a tabular summary example that includes only mandatory information, the tabular summary below highlights (bolded text) the mandatory information (although the specific format is not required). The summary may include optional contextual data (e.g., the time interval between the last dose received and the onset of the known

serious adverse event) in addition to the statutorily required information, and the sponsor or manufacturer may choose to submit this data if they believe the non-mandatory data could provide relevant information.

| Eligible investigational drug | IND number | Patient ID | Number of doses supplied | Number of patients treated | Disease(s) or condition(s) | Serious adverse event(s) | |
|-------------------------------|------------|------------|--------------------------|----------------------------|----------------------------|----------------------------------|----------------------------|
| | | | | | | Serious adverse event(s) | Outcome(s) |
| XDX501 | 99999 | 12345 | 5 | 1 | Breast cancer | 1. Hip fracture 2. Joint pain | 1. Improved 2. Improved |

F. Comments on Adverse Event Reporting

Some commenters made recommendations on proposed § 300.200(c)(5) regarding adverse event reporting. In that provision, we proposed to require that annual reports submitted to FDA include a tabular summary of any known serious adverse events, including resulting outcomes, experienced by patients treated with the eligible investigational drug under the Right to Try Act.

(Comment 6) One comment recommended that manufacturers and sponsors obtain data on the route of administration of the drug in the case of an adverse event.

(Response 6) While the Agency welcomes manufacturers or sponsors to include information they conclude is relevant to understanding a known serious adverse event, FDA believes we can adequately fulfill our public health role without including such a requirement; if FDA has questions about route of administration that are relevant to our review, we may pose such questions to manufacturers or sponsors.

FDA agrees that information on routes of administration may in some cases aid FDA in understanding the circumstances surrounding an adverse event. However, many drugs are not able to support multiple routes of administration, so for these drugs FDA may not gain any helpful information if we required reporting regarding route of administration.

(Comment 7) Some comments recommended that FDA encourage earlier reporting of known serious adverse events prior to the required due date for the annual summary.

(Response 7) FDA disagrees because section 561B(d)(1) of the FD&C Act directs that the reporting be “annual.” Nevertheless, we note that sponsors can always report safety data to FDA earlier than the timeframes required by this rule in accordance with § 312.32 (while also ensuring compliance with the reporting timeframes under this rule).

(Comment 8) One comment expressed concern with the definition of a “known serious adverse event,” arguing that only disclosing known serious adverse events is too limiting and will not provide enough information to evaluate a drug’s associated risks. Instead, the comment recommends that FDA require reporting of suspected adverse reactions. One comment also requested that FDA require manufacturers and sponsors to affirmatively seek information about known serious adverse events.

(Response 8) FDA disagrees with changing the proposed definition of “known serious adverse event” to encompass suspected serious adverse reactions. We consider suspected adverse reactions to be adverse events for which there is a reasonable possibility that the drug caused the adverse event (see, e.g., § 312.32(a) (defining “suspected adverse reaction”)). An adverse event, however, is any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related (see § 312.32(a)). Suspected adverse reactions are the subset of all adverse events for which there is a reasonable possibility that the drug caused the event. A “serious adverse event” is an adverse event that is “serious,” as defined in § 312.32(a). A “known serious adverse event” is a serious adverse event of which a manufacturer or sponsor is aware (§ 300.200(a)(4)). We believe it is appropriate to require that Right to Try annual summaries only include information about known serious adverse events for two reasons. First, Congress specifically required reporting of such events, but did not require that annual summaries include information about suspected adverse reactions. Second, at this time we do not see a need to require reporting under this rule for suspected adverse reactions because our IND safety reporting requirements in § 312.32 already require reporting of suspected adverse reactions and reflect the need for the sponsor to evaluate the available evidence. Accordingly,

FDA receives needed information about suspected adverse events through the IND safety reporting process.

With respect to the comment requesting that FDA require manufacturers or sponsors to affirmatively seek information about serious adverse events, we disagree. FDA does not seek to make this rule more burdensome than is needed to efficiently implement the Right to Try Act, and at this time it is not clear that any such investigation requirement would result in relevant information for purposes of FDA's Right to Try oversight role. Under the final rule, known serious adverse events must be reported. Nevertheless, sponsors are not constrained from including additional information they find to be relevant regarding a known serious adverse event.

G. Comments on the Definition of Manufacturer or Sponsor

In proposed § 300.200(a)(5), we proposed to define a “manufacturer or sponsor” as the person who meets the definition of “sponsor” in § 312.3 (21 CFR 312.3) for the eligible investigational drug; has submitted an application for the eligible investigational drug under section 505(b) of the FD&C Act (21 U.S.C. 355(b)) or section 351(a) of the Public Health Service Act (42 U.S.C. 262(a)); or produces the eligible investigational drug provided to an eligible patient on behalf of such persons.

(Comment 9) Some commenters made recommendations on proposed § 300.200(a)(5) regarding the definition of “manufacturer or sponsor.” One comment recommended the exclusion of contract manufacturing organizations from the term “manufacturer or sponsor” because a contract manufacturer may not possess the necessary information to complete the annual report. One comment requested that FDA limit the definition of “manufacturer or sponsor” to the treating physician because for drugs supplied through Right to Try, treating physicians are responsible for monitoring their patients' use of the drug and their safety.

(Response 9) FDA agrees that a contract manufacturing organization that is not closely connected to the clinical investigation and approval process should not be considered a

“manufacturer or sponsor” under this rule, and therefore we have updated the regulatory text to specify that a contract manufacturer is not a “manufacturer or sponsor.” We are making this change because we believe that only those entities that are closely connected to the clinical investigation or approval process should submit annual summaries, and contract manufacturers would generally not be considered such entities. A manufacturer or sponsor is better positioned to have access to the relevant data required for the annual summary if their role is not merely to manufacture a drug to another entity’s specifications on behalf of the other entity. Accordingly, we generally do not consider most contract manufacturers to be a “manufacturer or sponsor” for purposes of this rule. We consider a “contract manufacturer” to be an entity that merely manufactures a drug to another entity’s specifications on behalf of the other entity. We expect that whenever a drug is distributed under Right to Try, there will be a manufacturer or sponsor with access to the relevant data who will submit the required annual summary.

Regarding limiting the definition of “sponsor” to the treating physician, FDA disagrees because we think there will be less confusion if we use the regulatory definition of “sponsor” in § 312.3. This is a definition that industry and researchers are familiar with, and one that Congress likely understood when it used the term in the Right to Try Act. We also note that the Right to Try Act refers to “physician[s],” but not in the context of reporting annual summaries; rather, section 561B(a)(1) of the FD&C Act refers to “physician[s]” in the context of the definition of an eligible patient--suggesting that Congress understood “physician” and “sponsor” to not be synonymous.

(Comment 10) One comment requested that FDA require sponsors to include the physicians’ names and the total number of patients each physician has certified over each reporting period because of potential pressure for physicians to provide access to drugs under Right to Try.

(Response 10) FDA disagrees. Under section 561B(a) of the FD&C Act, the “eligible patient” definition provides for the certification by a physician; FDA information about the

identity of the physician is not needed for FDA to review the annual summary data as provided in the Right to Try Act. Therefore, FDA does not seek to require any information related to the physician.

(Comment 11) One comment requested that manufacturers assign patient identification numbers to track patients.

(Response 11) FDA recommends this practice only with respect to patients who experienced a known serious adverse event that is included in the Right to Try annual summary, to help distinguish between patients and events included in the annual summary. However, FDA does not believe it is necessary to require the assignment of patient identification numbers. Manufacturers or sponsors can take steps to ensure that they adequately track relevant safety information without the use of patient identification numbers, and if FDA has questions about information included in an annual summary FDA may contact the manufacturer or sponsor to clarify.

H. Comments on Reporting Patient Demographic Information

(Comment 12) Some commenters made recommendations regarding inclusion of patient demographic information. Some comments requested that the rule include a non-mandatory request for such other information to provide a more comprehensive picture on Right to Try use, such as the demographics of patients for whom Right to Try access was requested; information about requests that were denied, including reason for denial; amount charged for the product (if any); and overall patient outcomes from the Right to Try use. Other commenters asked for reporting of patient demographic information to be mandatory.

(Response 12) Congress specified the information FDA was to collect for the annual summary in the Right to Try Act and did not include demographic information. We encourage sponsors and/or manufacturers to provide demographic data, individual patient information, and other types of data suggested in the comments as optional additional contextual information when submitting the annual summary.

I. Comments on Outcomes Reporting

In proposed § 300.200(c)(5), we proposed to require that the annual summary include a tabular summary of any known serious adverse events, including resulting outcomes, experienced by patients treated with the eligible investigational drug under the Right to Try Act.

(Comment 13) One comment requested that FDA require manufacturers and sponsors to report all relevant clinical outcome data after treatment.

(Response 13) FDA disagrees. Congress did not specify that manufacturers or sponsors provide information about all treatment outcomes, and at this time we do not see a need to require this information in annual summaries. If FDA has questions about treatment outcomes not associated with known serious adverse events, FDA can request that information as appropriate.

(Comment 14) One comment disagreed with the proposed requirement that annual summaries include information about outcome data. The comment stated that patients who receive drugs under Right to Try are being treated individually and not as a part of a clinical trial, so treatment plans may vary.

(Response 14) We disagree. The proposed requirement is to report any known serious adverse events, including resulting outcomes; the outcomes are tied specifically to the adverse event, and not the outcome of each individual use of an eligible drug, as the comment suggests. Requiring information about outcomes resulting from known serious adverse events is important so that FDA can meet the directive in section 561B(d)(2) of the FD&C Act, that FDA shall post an annual summary report including information specific to “clinical outcomes.” See section 701(a) of the FD&C Act (providing FDA with authority to promulgate regulations for the efficient enforcement of the FD&C Act). In addition, the outcome of the adverse event can provide important context to enable FDA to determine if the outcomes are critical to understanding safety issues associated with the eligible investigational drug without requesting

additional information for each event. We also note that the Agency routinely evaluates safety outcomes outside of a clinical trial, so just because eligible patients may not be part of a clinical trial does not mean we are unable to review information about their outcomes.

(Comment 15) One comment requested more information on how the Secretary of Health and Human Services would inform sponsors that the Agency's use of a drug's clinical outcome is critical to making a safety determination on the use of the drug.

(Response 15) This comment relates to section 561B(c) of the FD&C Act, which includes certain restrictions on certain FDA uses of a clinical outcome associated with Right to Try unless FDA makes a determination that use of such clinical outcome is critical to determining the safety of the eligible investigational drug. If FDA makes such a determination, section 561B(c)(2) of the FD&C Act provides that FDA "shall provide written notice of such determination to the sponsor, including a public health justification for such determination, and such notice shall be made part of the administrative record." FDA does not believe additional clarification is necessary because the statute specifies that FDA's notification to the sponsor shall be "written." The comment has not explained what additional clarification is needed.

J. Comments on the Clarity of the Proposed Rule

(Comment 16) One comment requested an explicit statement from FDA that there are no reporting requirements for sponsors or manufacturers who choose not to grant a request to provide products under Right to Try.

(Response 16) FDA is not sure what kind of explicit statement the comment seeks. Neither the Right to Try Act nor this final rule require parties to report to FDA when they have declined to distribute drugs under the Right to Try Act. FDA notes that there is no requirement that a manufacturer or sponsor participate in Right to Try.

(Comment 17) One comment requested clarity on whether an annual summary is only required if new access to a drug has been granted during the reporting period or if sponsors should also report on ongoing use from a prior reporting period.

(Response 17) Under § 300.200(c)(2), the manufacturer or sponsor must report the total number of doses supplied. The relevant period of time is the period of time covered by the annual summary. Therefore, the number of doses supplied during the annual summary period is what should be reported. For example, if Patient A started using the drug in the previous reporting period and continues to use that drug in the current reporting period, the manufacturer or sponsor should report how many doses were supplied during the current reporting period.

(Comment 18) One comment requested that FDA consider providing criteria on how a patient would submit a request for a drug under Right to Try.

(Response 18) The Right to Try Act does not outline a role for FDA with respect to the process by which patients may request access to eligible investigational drugs. Therefore the comment asks FDA to provide information about a matter that is beyond the scope of this rulemaking. We decline.

(Comment 19) One comment requested additional detail on FDA's intent to post online an annual summary report and expressed interest in how FDA's posting of the annual summary report "may increase awareness about the availability of investigational drugs" as noted in the "Costs and Benefits" section of the preamble to the Proposed Rule. One comment also stated that the information FDA includes in the annual summary report does not convey or imply any conclusions regarding the safety or efficacy of the products provided under the Right to Try Act, and it may also be helpful for FDA's annual summary report website to link to additional information regarding "Expanded Access."

(Response 19) FDA will follow the requirements in the Right to Try Act regarding posting an annual summary of uses of drugs under the statute. As stated in the preamble to the proposed rule, providing this information will increase awareness about the availability of investigational drugs because the report will make available data about the use of eligible investigational drugs. With respect to the comment stating that the information included in FDA's annual summary report will not convey or imply any conclusions about a drug's safety or

efficacy, we agree. The information included in FDA’s annual summary reports will be purely factual and will not reflect any FDA evaluations of the eligible investigational drugs. With respect to the comment requesting that our website link to information about “Expanded Access,” we will consider that comment when we design our website for Right to Try annual summary reports.

V. Effective/Compliance Date(s)

This final rule becomes effective 60 days after publication in the *Federal Register*. Any manufacturer or sponsor who provides an eligible investigational drug for use by an eligible patient in accordance with the Right to Try Act must include in their first annual summary submitted under this section any use from the time of enactment of the Right to Try Act, May 30, 2018, through December 31, 2022. The first annual summary submitted under the Right to Try Act will be required to be submitted March 31, 2023.

Thus, for a manufacturer or sponsor of an eligible investigational drug that has supplied an eligible patient with an eligible investigational drug under section 561B of the FD&C Act between the period from enactment of section 561B (May 30, 2018) and December 31, 2022, the manufacturer or sponsor shall submit to FDA a first annual summary covering that period no later than March 31, 2023. After this annual report, the manufacturer or sponsor must submit a report that covers every January 1 through December 31 annual period by no later than March of the following year, for every year in which the manufacturer or sponsor has supplied a drug under the Right to Try Act. Therefore, a report submitted in March 2024, would cover the period January 1, 2023, through December 31, 2023.

VI. Economic Analysis of Impacts

A. Introduction

We have examined the impacts of the final rule under Executive Order 12866, Executive Order 13563, the Regulatory Flexibility Act (5 U.S.C. 601-612), and the Unfunded Mandates Reform Act of 1995 (Pub. L. 104-4). Executive Orders 12866 and 13563 direct us to assess all

costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). We find that this final rule is not a significant regulatory action as defined by Executive Order 12866.

The Regulatory Flexibility Act requires us to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because the effects are low in cost and minimally dispersed, we certify that the final rule will not have a significant economic impact on a substantial number of small entities.

The Unfunded Mandates Reform Act of 1995 (section 202(a)) requires us to prepare a written statement, which includes an assessment of anticipated costs and benefits, before issuing “any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of \$100,000,000 or more (adjusted annually for inflation) in any one year.” The current threshold after adjustment for inflation is \$165 million, using the most current (2021) Implicit Price Deflator for the Gross Domestic Product. This final rule would not result in an expenditure in any year that meets or exceeds this amount.

B. Summary of Costs and Benefits

This final rule implements a statutory requirement in the Right to Try Act that sponsors and manufacturers who provide an eligible investigational drug under the Right to Try Act to eligible patients submit to FDA an annual summary of such use. The Right to Try Act requires FDA to specify by regulation the deadline and requires that submissions include certain information.

The benefits of this final rule consist of societal and public health outcomes that may accrue from the disclosure of the use of investigational drugs and any known serious adverse events provided in these annual summary reports. These reporting requirements instruct firms to collect all known serious adverse events and submit them once per year to FDA. Without these

reports, FDA would not be made aware in a systematic manner of the use of eligible investigational drugs under the Right to Try Act and any known serious adverse events. With these reports, there may be increased awareness of investigational drugs, the diseases or conditions for which patients are seeking access, and any known serious adverse events associated with such use.

In addition, based on the information in these annual summaries, FDA intends to post an annual summary report in accordance with section 561B(d)(2) of the FD&C Act. FDA's posting of these reports may increase awareness about the availability of investigational drugs. In some cases, access to such drugs may help treat future patients. There is no data that would allow us to predict the magnitude of generated benefits, and thus we are unable to quantify the expected benefits of this rule.

Costs are calculated as the time spent by firms to prepare and submit annual summary reports based on participation in Right to Try Act requests from eligible patients for investigational new treatments. The total estimated present value of this rule's costs is \$37,132 at a 7 percent discount rate and \$45,818 at a 3 percent discount rate (in 2020 dollars). The annualized cost of this rule over 10 years is \$5,287 at a 7 percent discount rate and \$5,371 at a 3 percent discount rate. Consistent with Executive Order 12866, table 1 provides the costs and a description of benefits for this final rule over a 10-year period.

Table 1.--Summary of Benefits, Costs, and Distributional Effects of the Final Rule

| Category | | Primary Estimate | Low Estimate | High Estimate | Units | | | Notes |
|----------|------------------------------|---|--------------|---------------|--------------|---------------|----------------|-------|
| | | | | | Year Dollars | Discount Rate | Period Covered | |
| Benefits | Annualized Monetized \$/year | | | | 2020 | 7% | 10 | |
| | | | | | 2020 | 3% | 10 | |
| | Annualized Quantified | | | | | 7% | | |
| | | | | | | 3% | | |
| | Qualitative | Disclosure of known serious adverse events and outcomes related to investigational new drug treatments. | | | | | | |
| Costs | Annualized Monetized \$/year | \$5,287 | | | 2020 | 7% | 10 | |
| | | \$5,371 | | | 2020 | 3% | 10 | |
| | Annualized Quantified | | | | | 7% | | |
| | | | | | | 3% | | |

Table 1.--Summary of Benefits, Costs, and Distributional Effects of the Final Rule

| | | | | | | | | |
|-----------|--------------------------------------|-------|--|--|-----|----|--|--|
| | Qualitative | | | | | | | |
| Transfers | Federal Annualized Monetized \$/year | | | | | 7% | | |
| | | | | | | 3% | | |
| | From/To | From: | | | To: | | | |
| | Other Annualized Monetized \$/year | | | | | 7% | | |
| | | | | | | 3% | | |
| | From/To | From: | | | To: | | | |
| Effects | State, Local or Tribal Government: | | | | | | | |
| | Small Business: | | | | | | | |
| | Wages: | | | | | | | |
| | Growth: | | | | | | | |

We have developed a comprehensive Economic Analysis of Impacts that assesses the impacts of the final rule. The full analysis of economic impacts is available in the docket for this final rule (Ref. 1) and at <https://www.fda.gov/about-fda/reports/economic-impact-analyses-fda-regulations>.

VII. Analysis of Environmental Impact

We have determined under 21 CFR 25.30(h) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

VIII. Paperwork Reduction Act of 1995

This final rule contains information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3521). The title, description, and respondent description of the information collection provisions are shown in the following paragraphs with an estimate of the annual reporting burden. Included in the estimate is the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing each collection of information.

Title: Annual Summary Reporting Requirements Under the Right to Try Act--21 CFR Part 300, subpart D--OMB Control Number 0910-NEW.

Description: The final rule provides for a submission schedule and sets forth content requirements for sponsors and manufacturers who: (1) provide an eligible investigational drug for use by an eligible patient and (2) submit to FDA an annual summary report by subject to the applicable regulations.

Regulations in § 300.200 require that sponsors and manufacturers submit to FDA an annual summary no later than March 31 of each year, including data for the preceding calendar year, which is the period from January 1 through December 31. The first report will cover the time period between enactment of the Right to Try Act (March 30, 2018) and December 31, 2022. We will provide instruction on the FDA Right to Try web page at <https://www.fda.gov/patients/learn-about-expanded-access-and-other-treatment-options/right-try> regarding a designated point of contact for submissions of Right To Try annual reporting summaries and are currently developing a form to facilitate submission of requisite information. Data elements included in the annual summary are:

- The name of the eligible investigational drug and applicable IND number.
- The number of doses supplied to the eligible patient.
- The number of eligible patients treated.
- The use for which the eligible investigational drug was made available to the eligible patient.
- Any known serious adverse events and outcomes that the eligible patient treated with an eligible investigational drug experienced.

Description of Respondents: Respondents to the information collection are sponsors and manufacturers who provide an eligible investigational drug to eligible patients in accordance with the Right to Try Act and will submit to FDA annual summaries.

As discussed in section II.F of the Final Regulatory Impact Analysis, we estimate the burden of the information collection as follows:

Table 2.--Estimated Annual Reporting Burden¹

| Activity; 21 CFR Citation | No. of Respondents | No. of Responses per Respondent | Total Annual Responses | Average Burden per Response (in hours) | Total Hours |
|--|--------------------|---------------------------------|------------------------|--|-------------|
| Sponsors and manufacturers submit annual summaries in accordance with the Right to Try Act (§ 300.200) | 6 | 1 | 6 | 2.5 | 15 |

¹There are no capital costs or operating and maintenance costs associated with this collection of information.

Consistent with estimates in our Final Regulatory Impact Analysis, we estimate that six sponsors and manufacturers will prepare and submit six annual summaries and assume it takes 2.5 hours to prepare and submit each summary, which results in a total of 15 hours annually.

The information collection provisions in this final rule have been submitted to OMB for review as required by section 3507(d) of the Paperwork Reduction Act of 1995.

Before the effective date of this final rule, FDA will publish a notice in the *Federal Register* announcing OMB's decision to approve, modify, or disapprove the information collection provisions in this final rule. An Agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

IX. Federalism

We have analyzed this final rule in accordance with the principles set forth in Executive Order 13132. We have determined that the rule does not contain policies that have substantial direct effects on the States, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of government. Accordingly, we conclude that the rule does not contain policies that have federalism implications as defined in the Executive Order and, consequently, a federalism summary impact statement is not required.

X. Consultation and Coordination with Indian Tribal Governments

We have analyzed this rule in accordance with the principles set forth in Executive Order 13175. We have determined that the rule does not contain policies that have substantial direct effects on one or more Indian Tribes, on the relationship between the Federal Government and

Indian Tribes, or on the distribution of power and responsibilities between the Federal Government and Indian Tribes. Accordingly, we conclude that the rule does not contain policies that have tribal implications as defined in the Executive Order and, consequently, a tribal summary impact statement is not required.

XI. Reference

The following reference is on display at the Dockets Management Staff (see ADDRESSES) and is available for viewing by interested persons between 9 a.m. and 4 p.m., Monday through Friday, 240-402-7500; it is also available electronically at <https://www.regulations.gov>. FDA has verified the website address, as of the date this document publishes in the *Federal Register*, but websites are subject to change over time.

1. Economic Analysis of Impacts (available at <https://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/EconomicAnalyses/default.htm>)

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List of Subjects in 21 CFR Part 300

Drugs, Prescription drugs.

Therefore, under the Federal Food, Drug, and Cosmetic Act, and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 300 is amended as follows:

PART 300--GENERAL

1. The authority citation for part 300 is revised to read as follows:

Authority: 21 U.S.C. 331, 351, 352, 355, 360b, 360bbb-0a, 371.

2. Add subpart D, consisting of § 300.200, to read as follows:

Subpart D--Annual Summary Reporting Requirements.

§ 300.200 Annual summary requirements under the Right to Try Act.

(a) Definitions: The following definitions of terms apply only to this section:

(1) *Eligible investigational drug*. An eligible investigational drug is as defined in section 561B(a)(2) of the Federal Food, Drug, and Cosmetic Act.

(2) *Eligible patient.* An eligible patient is as defined in section 561B(a)(1) of the Federal Food, Drug, and Cosmetic Act.

(3) *Investigational New Drug (IND).* An IND is as defined in § 312.3 of this chapter.

(4) *Known serious adverse event.* A serious adverse event (as defined in § 312.32 of this chapter) is considered “known” if the manufacturer or sponsor is aware of it.

(5) *Manufacturer or sponsor.* A manufacturer or sponsor is the person who:

(i) Meets the definition of “sponsor” in § 312.3 of this chapter for the eligible investigational drug;

(ii) Has submitted an application for the eligible investigational drug under section 505(b) of the Federal Food, Drug, and Cosmetic Act or section 351(a) of the Public Health Service Act; or

(iii) Is other than a contract manufacturer acting on behalf of a manufacturer or sponsor, producing the eligible investigational drug provided to an eligible patient on behalf of the persons described in paragraph (a)(5)(i) or (ii) of this section.

(b)(1) Except as described in paragraph (b)(2) of this section, a manufacturer or sponsor of an eligible investigational drug shall submit to the Food and Drug Administration (FDA), no later than March 31 of each year, an annual summary of any use of eligible investigational drugs supplied to any eligible patient under section 561B of the Federal Food, Drug, and Cosmetic Act for the period of January 1 through December 31 of the preceding year.

(2) For a manufacturer or sponsor of an eligible investigational drug that has supplied an eligible patient with an eligible investigational drug under section 561B of the Federal Food, Drug, and Cosmetic Act between the period from enactment of section 561B (May 30, 2018) and December 31, 2022, the manufacturer or sponsor shall submit to FDA a first annual summary covering that period no later than March 31, 2023.

(c) For each eligible investigational drug, the annual summary must include:

(1) *The name of the eligible investigational drug and applicable IND number.* The name and IND number of the eligible investigational drug supplied by the manufacturer or sponsor for use under section 561B of the Federal Food, Drug, and Cosmetic Act.

(2) *Number of doses supplied.* The total number of doses supplied by the manufacturer or sponsor to eligible patients for use under section 561B of the Federal Food, Drug, and Cosmetic Act. Each dose of an eligible investigational drug supplied for an eligible patient shall be counted as a dose supplied.

(3) *Number of patients treated.* The total number of eligible patients for whom the manufacturer or sponsor provided the eligible investigational drug for use under section 561B of the Federal Food, Drug, and Cosmetic Act. An eligible patient treated more than one time or with multiple doses of an eligible investigational drug shall be counted as a single patient.

(4) *Use for which the eligible investigational drug was made available.* A tabular summary identifying the diseases or conditions for which the eligible investigational drug was made available for use under section 561B of the Federal Food, Drug, and Cosmetic Act.

(5) *Any known serious adverse events and outcomes.* A tabular summary of any known serious adverse events, including resulting outcomes, experienced by patients treated with the eligible investigational drug under section 561B of the Federal Food, Drug, and Cosmetic Act.

(d) Annual summaries submitted pursuant to this section shall be submitted in an electronic format that FDA can process, review, and archive, and shall be sent directly to a designated point of contact for submissions made under section 561B of the Federal Food, Drug, and Cosmetic Act. The annual summaries must be submitted to the designated point of contact and shall not be submitted to a particular investigational new drug application. FDA will specify the designated point of contact for submission of the annual summary on FDA's website, as described at <https://www.fda.gov>.

Dated: August 31, 2022.

Robert M. Califf,

Commissioner of Food and Drugs.

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